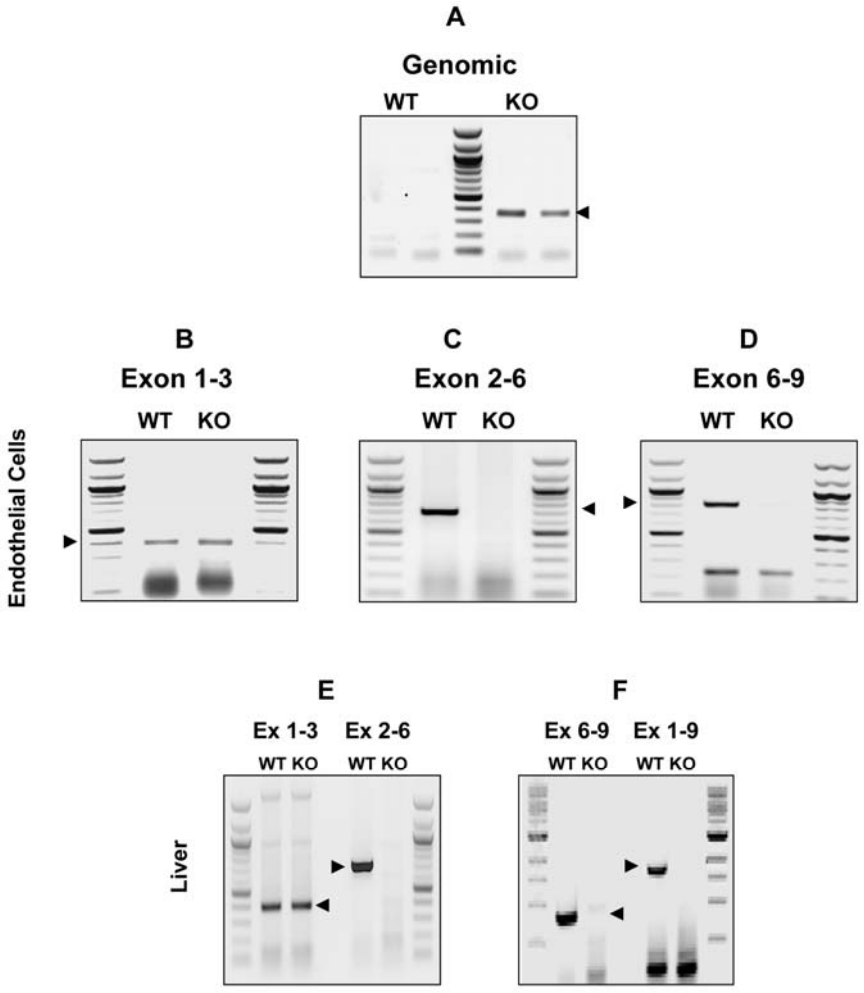
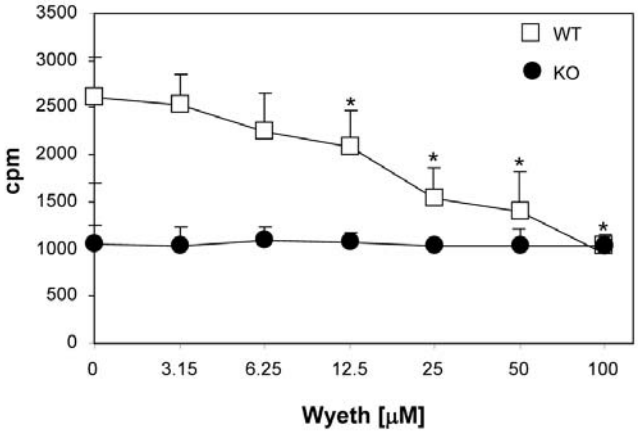
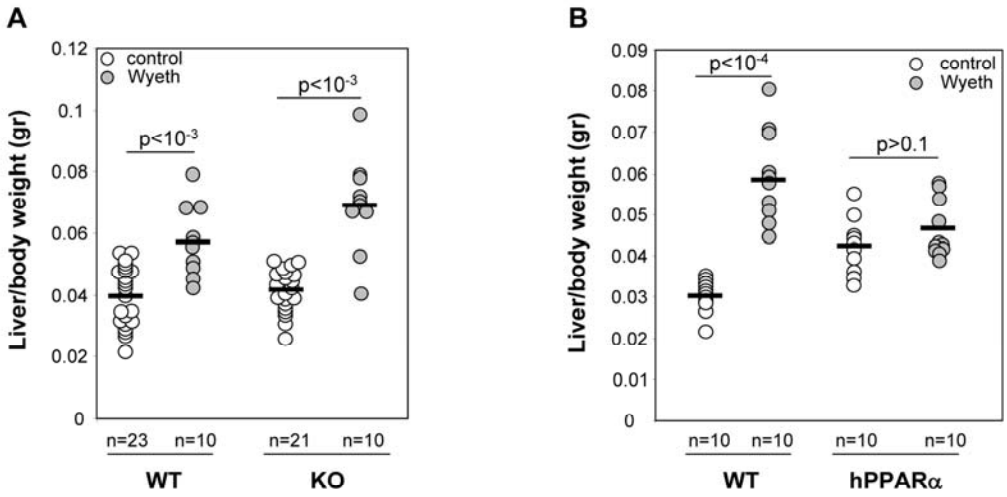


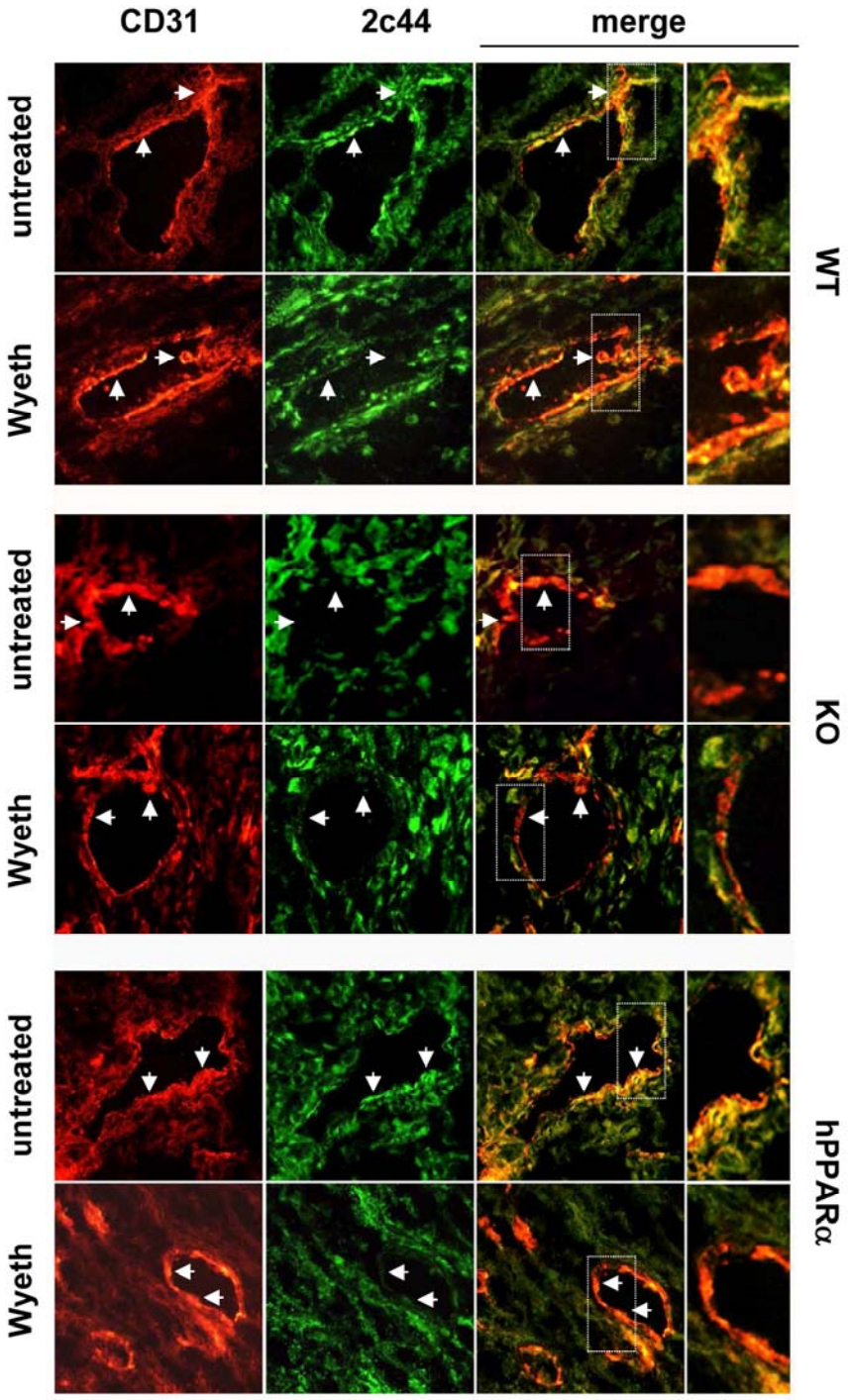
Supplementary Figure 1: Characterization of Cyp2c44(-/-) mice by PCR amplification of genomic DNA and of DNAs reversed transcribed from endothelial cell and liver RNAs. **(A):** PCR amplification of tail DNAs from wild type (WT) and *Cyp2c44(-/-)* (KO) mice using diagnostic PCR primers flanking the viral trap insertion site in exon 4, and the 3'-end of the trap (5'-ttacgactgagccacattcc-3' and 5'-ggcgttacttaagctagcttgc) (350 bp). **(B-F):** PCR amplification of reversed transcribed RNAs from cultured lung endothelial cells and livers from WT and KO mice using PCR primers designed to amplify the following segments of the Cyp2c44 mRNA: **B** and **E:** exon 1 to 3 (5'-gacatggagctgctgggtct-3' and 5'-ggagaagcgtcgcaggagtt-3') (398 bp); **C** and **E:** exon 2 to 6 (5'-ttggatcctggcctaccgtg-3' and tgtctctgtgcctgccgtaa-3')(680 bp); **D** and **F:** exon 6 to 9 (5'-ccttgtcaagcatccagagg-3' and 5'-tgaagccacagaagagcacg-3') (822 bp); **F:** exon 1 to 9 (5'-gacatggagctgctgggtct-3' and 5'-atcggtgtcagttgtgctt-3') (1713 bp). The arrows indicate the mobility of each PCR product.



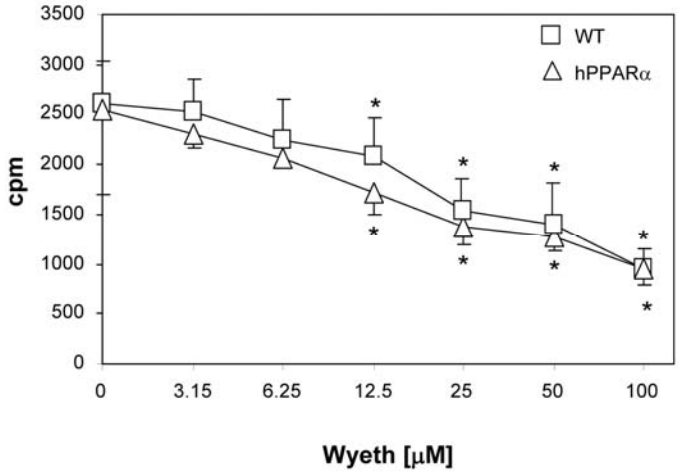
Supplementary Figure 2: Wyeth fails to inhibit the proliferation of Cyp2c44 KO endothelial cells. Micro-vascular endothelial cells, isolated from the lungs of WT or KO mice, were cultured in medium containing 2.5% FCS with our without Wyeth at the indicated concentrations. Two days later, the cells were incubated with [^{3}H]thymidine (1 μC/well) and their proliferation determined as described in Methods. Values shown are averages ± SD of 3 experiments performed in quadruplicate. (*) indicates significant differences ($p<0.05$) between untreated and Wyeth-treated cells.



Supplementary Figure 3: The administration of Wyeth causes liver hypertrophy in WT and Cyp2c44 KO, but not PPARα humanized (hPPARα) mice. **(A, B)** Groups of WT, KO, and hPPARα mice were left untreated (control) or administered Wyeth (0.02% v/v) in their drinking water for a period of 16 days. The ratios of liver mass to body weight were used as estimates of the extent liver hypertrophy. Shown are individual liver/body weight ratio (circles) and averages (solid lines).



Supplementary Figure 4*:* The administration of Wyeth causes down-regulation of endothelial Cyp2c44 in tumors from WT and PPARα humanized (hPPARα) mice*.*** Frozen sections of tumors derived from the mice indicated were co-stained with rat anti-mouse CD31 (red) and rabbit anti-mouse Cyp2c44 (green). Images were subsequently merged to visualize endothelial expression of Cyp2c44 (yellow). Note that in tumors derived from untreated *Cyp2c44(-/-)* (KO) or Wyeth-treated WT, KO, and *hPPARα* mice, Cyp2c44 staining is only and/or primarily localized to the tumor parenchyma (green). In contrast, in untreated WT and hPPARα mice, Cyp2c44 staining is localized both in tumor (green) and endothelium (yellow).



Supplementary Figure 5: Wyeth inhibits the proliferation of PPARα humanized (hPPARα) endothelial cells. Micro-vascular endothelial cells, isolated from the lungs of WT or hPPARα mice, were cultured in medium containing 2.5% FCS with our without Wyeth at the indicated concentrations. Two days later, the cells were incubated with [^{3}H]thymidine (1 µC/well) and their proliferation determined as described in Methods. Values shown are averages ± SD of 1 experiment performed in quadruplicate. (*) indicates significant differences ($p<0.05$) between untreated and Wyeth-treated cells.

	Untreated		Wyeth-treated	
Regioisomer	**WT**	**KO**	**WT**	**KO**
8,9-EET	2.0 ± 0.3[a]	2.2 ± 0.2[e]	0.8 ± 0.1	0.9 ± 0.2
11,12-EET	1.2 ± 0.3[b]	1.4 ± 0.2[f]	0.8 ± 0.3	0.7 ± 0.2
14,15-EET	1.9 ± 0.1[c]	1.8 ± 0.3[g]	1.2 ± 0.1	1.0 ± 02
TOTAL	5.1 ± 0.3[d]	5.4 ± 0.2[h]	2.8 ± 0.5	2.6 ± 0.5

Supplementary Table 1: Effects of Cyp2c44 gene disruption on the plasma EETs of untreated and Wyeth- treated mice*.* Male wild type (WT) and *Cyp2c44(-/-)* KO mice were administered either water or an aqueous solution of Wyeth14,643 (0.02% w/v) as their source of drinking liquid. After 8-10 days, plasma samples were obtained by form EDTA collected blood, and the EETs extracted, purified, and quantified by LC/MS/MS as described in Methods. Values are given as ng of EET/ml of plasma, and are averages ± SE calculated from 4 different experiments. Significantly different between WT or KO untreated or Wyeth-treated with $p \leq$ than: a, 0.02; b, 0.01; c, 0.01; d, 0.06; e, 0.04; f, 0.05; and g, 0.001. The differences between WT and KO either untreated or Wyeth-treated were non-significant ($p > 0.05$).